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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,071	05/08/2001	Ann Marie Schmidt	0575/55424-Z/JPW/SHS/MVM	3248

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/851,071	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ they raise the issue of new matter (see Note below);
   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____.
3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *17,19-21,34 and 35*.

   Claim(s) withdrawn from consideration: _____.
8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

JEFFREY FREDMAN
PRIMARY EXAMINER

Continuation of 5. does NOT place the application in condition for allowance because:

Claims 17, 19-21 and 34 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Chintala et al (Cancer Lett 103:21-208, 1996), for the same reasons of record as set forth in the office action mailed on 09/26/03.

The applicant argues that Chintala fails to teach each and every element of the claimed method. Rather, Chintala teaches that when two gliablastoma cell lines, SNB19 and U251, are treated with antibodies to $\alpha 3\beta 1$ and $\alpha 5\beta 1$ integrins, there is an increase in the invasive ability of the tumor cells. Chintala fails to teach the instant method for evaluating the ability of an agent to inhibit tumor cell spreading. Accordingly, applicants maintain that Chintala fails to anticipate the claimed invention.

However, this is found NOT persuasive because the invasive assay disclosed on page-203 of instant reference clearly anticipates all the elements of the invention as claimed. The invasive ability of the SNB19 and U251 human glioma cells in-vitro was measured by the invasion of cells through metrigel in 48-well microchemotaxis chamber (page 203, col.1 para.1; page 204, fig-2; page 205, fig 3, 4; page 207, fig-7). The invasive assay disclosed teaches the treatment of cells with candidate agents, which encompasses the step a) and b) of claim 17. Furthermore the invasive assay determines the spread of tumor cells by counting the cells, which passed through the matrigel to the lower side of the filter. This clearly anticipate the step c) of claim 17. The cited art teaches the comparative evaluation of BSA, Coll IV, Fibronectin and Laminin in cell migration, which clearly anticipate the step b) of claim 1. In addition cited art teaches RGD inhibits the interaction of glioblstoma cell lines with fibronectin in a dose dependent fashion (page 203, col.2). Even though the cited art does not specifically identify agents that inhibit tumor invasion, screening of such a compound using the disclosed invasive assay is well within the reach of one skill in the art. Since the invasive assay of Chintala can be used to evaluate the ability of an agent that modulates (increase or decrease) tumor cell spreading, the invasive assay as disclosed in the cited art of record clearly anticipate the invention as claimed. Therefore given the broadest reasonable interpretation the Invasive Assay as taught by the cited art clearly anticipates all elements of the claimed invention.

Claims 17, 19-21 and 34-35 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Softer et al (PNAS 89:1557-1561, 1992), for the same reasons of record as set forth in the office action mailed on 09/26/03.

The applicant argues that Seftor fails to teach each and every element of the claimed method. Rather, Seftor teaches that when A375M human melanoma cells are treated with antibodies to the $\alpha 3\beta 1$ integrin or soluble vitronectin, there is an increase in the invasive ability of the tumor cells. Like Chintala, Seftor fails to teach the instant method for evaluating the ability of an agent to inhibit tumor cell spreading. The examiner has not clearly set forth how this reference teaches each and every step of the claimed method. Accordingly, applicants maintain that Seftor fails to anticipate the claimed invention.

However, this is found NOT persuasive because the cited art clearly teaches an in-vitro invasion assay system, wherein in the assay was performed in membrane invasion culture system (MICS) using polycarbonate filter containing 10um pores coated with Metrigel. The cited art further teaches the determination of invasion potential of the treated and untreated tumor cells (page 1558, col.1 para.2, page 1559, fig-3). Figure-3 clearly teaches the evaluation of invasiveness of A375M melanoma cells with or without treatment with anti-integrin antibody ($\alpha V\beta 3$ integrin). The cited art further teaches the inoculation of fresh antibody daily throughout the course of 72-hr assay. Even though the cited art does not specifically teach agents that inhibit tumor invasion, screening of such a compound using the disclosed invasion culture system (MICS) is well within the reach of one skill in the art. Since the invasion culture system of Seftor can be used to evaluate the ability of an agent that modulates (increase or decrease) tumor cell spreading, the invasion culture system as disclosed in the cited art clearly anticipate the invention as claimed.